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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/975,456	10/11/2001	Michel Lazdunski	1478-R-00	9176

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EXAMINER
NASHED, NASHAAT T

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/975,456	Applicant(s) Lazdunski et al.
	Examiner Nashaat T. Nashed	Art Unit 1652

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 13, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above, claim(s) *4-10 and 14-19* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3 and 11-13* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicant's election without traverse of Group I, claims 1-3 and 11-13, in Paper No. 13 is acknowledged. Claims 4-10 and 14-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim.

Claims 11-13 are objected to because they contain non-elected subject matter of claim 4. The claims will be examined to the extend necessary to properly examine the elected subject matter.

The disclosure is objected to because of the following informalities:

(a) The reference to International Patent Application on page 2, second paragraph, is improper because it does not identify the country to which the application was filed. It is recommended to use a publication number, i. e., a WO publication number if available.

(b) Figure 1 contains nucleic/amino acid sequences which are not identified by a sequence identification numbers in the Figure or the Figure's description. Applicant must perfect the specification compliance with the sequence rule.

(c) GenBan accession numbers have been detected in the specification referencing specific nucleic/amino acid sequences, see for example page 3, paragraph 3; page 10, paragraph 3; and page 15, last paragraph. Referencing specific nucleic/amino acid sequences by accession numbers of a commercial data base is not permissible because the data base may change the accession numbers without referring back to the original numbers. Applicants must identify the accession numbers by a sequence identification numbers and perfect the application compliance with the sequence rule. Applicants may be required to file a new sequence listing and a computer readable form (CRF), if the nucleic/amino acid sequences of the referenced GenBank accession numbers are not part of the sequence listing and the CRF.

(d) The abbreviation "POPS" is not defined in the specification.

Appropriate correction is required.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1-3 are rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter.

In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter. *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims to contain wording such as "An isolated and purified protein or nucleic acid". It should be noted that a recombinant enzymes/proteins are assumed to be identical to those produced naturally unless otherwise indicated.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, and 11-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and its dependent claims 3 and 11-13 are directed to all mammalian secreted group IIF sPLA2 with the recited characteristics in claim 1. The specification, however, only provides a single representative species from human encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of these Group IIF sPLA2 by any identifying structural characteristics or properties other than the activities recited in claim 1, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claims 1, 3 and 11-14 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to an isolated Group IIF calcium ion

dependent phospholipase A of SEQ ID NO: 2 and composition thereof. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to all possible mammalian calcium ion dependent phosphlipases and the composition thereof which treat and/or prevent viral, bacterial diseases as well as cancer. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any mammalian Group IIF calcium ion-dependent phospholipase, and pharmaceutical composition thereof for the treatment of viral and bacterial diseases as well as cancer. The specification provides guidance and examples in the form of an assay to clone the human gene encoding SEQ ID NO: 2, express the polypeptide, and isolate the polypeptide of SEQ ID NO: 2 and characterize its catalytic activity (see the specification pages 10-13, and 18). The specification fails to teach any specific biological role/function for the claimed enzyme or its relationship to any viral and bacterial diseases as well as cancer. While molecular biological techniques and genetic manipulation to make any polypeptide are known in the prior art and the skill of the artisan are well developed, knowledge regarding the structure and function of all possible phosphlipases having the characteristic cited in claim 1 is lacking. Also, formulating a pharmaceutical composition to treat some diseases from a polypeptide is within the ordinary skilled artesian, the use of such a composition is not. Thus, searching for a gene encoding a phospholipase and making and using the said phospholipase A2 is well outside the realm of routine experimentation and predictability in the art of success is extremely low. The amount of experimentation to isolate such a gene and characterize its catalytic activities and properties as well as the amount of experimentation required to identify a viral, bacterial diseases or a cancer which can be treated by said polypeptide is enormous. Since routine experimentation in the art does not include screening genomic or cDNA libraries or screening for the use of composition of the polypeptide in the treatment of viral or bacterial diseases, or a cancer where the expectation of obtaining the desired phospholipase A2 or identifying the desired disease for treatment is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding any structural bases for the cited properties in claim 1, DNA and/or amino acid sequence homologies among the various members of the claimed genus, the biological function of the polypeptide or a specific association between the polypeptide(s) and a specific cancer, or viral or bacterial disease. Without such a guidance, the experimentation left to those skilled in the art is undue.

Claims 1-3 and 11-13 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

(a) claims 1-3 contains the undefined abbreviations and acronyms sPLA2. Abbreviations and acronyms must be defined at least once in the claims.

(b) the phrase "hydrolyzes phosphatidylglycerol versus phosphatidylcholin with about a 15-fold preference" in claim 1 render the claim indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. The claim is found indefinite because the catalytic preference may vary with the conditions and the specific substrates used to measure the activities, and what is being compared. For examination purposes only, the limitation has been deleted. Applicants may over come this rejection by inserting the names of the specific substrates used and other reaction conditions found in the paragraph bridging pages 12 and 13.

(c) claims 11-13 are included in this rejection because they are dependent on a rejected claim and do not cure its deficiencies.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3 and 11-13 are rejected under 35 U.S.C. § 102(a) as being anticipated by Valentine *et al.* [Valentine, J. Biol. Chem. 274 (44), 31195-31202 (1999)].

Valentine teach the cloning and expression of a secreted phospholipase A2 from mouse which belongs to Group FII sPLA2. The amino acid sequence taught by Valentine for Group FII sPLA2 is shown in Figure 1 aligned with other mouse phospholipase A2, and have 78% sequence homology to SEQ ID NO: 2 of the instant application. The pH optimum of the mouse FII sPLA2 is about 7, see Figure 4. Also the FII sPLA2 taught by

Valentine has preference in hydrolyzing phosphatidylglycerol when compared to phosphatidylcholine (claims 1 and 3). Also, Valentine teach sPLA2s have antibacterial activity and act as tumor suppressor in colorectal cancer (claims 11-13)

Claims 1-3 and 11-13 are rejected under 35 U.S.C. § 102(e) as being anticipated by Das *et al.* (Das, WO 01/85956-A2).

Das teach the amino acid sequence of SEQ ID NO: 2 [named Human Lipid Metabolizing enzyme-2, LME-2, and Incyte polypeptide ID # 7473224CD1] comprising the amino acid sequence of the instant application (claims 1-3). Residues 44-211 of the sequence disclosed by Das is identical to SEQ ID NO: 2 of the instant application. In table 2, it is indicated that the polypeptide of SEQ ID NO: 2 is a Group IIF secreted phospholipase A2, and indicated that it is the human analog of the mouse enzyme reported by Valentine *et al.* [J. Biol. Chem. 274 (44), October 29, 31195-31202 (1999)]. The pH optimum and the substrate preference for the polypeptide disclosed by Das are intrinsic properties of said polypeptide. Also, Das teach that the catalytic activities of phospholipases are calcium ion-dependent, see page 7, paragraph 3. In addition, Das teach a composition containing the polypeptide of SEQ ID NO: 2 of various cancers and viral caused diseases such as AIDS (claims 11-13), see pages 43 and 44.

WO 01/85956-A2 is a published international application, PCT/US01/15210, filed May 11, 2001 in the United States and claim priority to provisional application 60/203,511, filed May 11, 2000, which enable the amino sequence of SEQ ID NO: 2.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Valentin *et al.* "Cloning and recombinant expression of human group IIF-secreted phospholipase A2" Biochem. Biophys. Res. Commu. **279**, 223-228 (2000).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is (703) 305-6586. The examiner can normally be reached Monday, Tuesday, Thursday, and Friday from 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone numbers for this Group are (703) 305-3014 and (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nashaat T. Nashed, Ph. D.
Primary Examiner